Durability of Efficacy and Safety of Roflumilast Cream 0.3% in Adults With Chronic Plaque Psoriasis From a 52-Week, Phase 2 Open-Label Safety Trial

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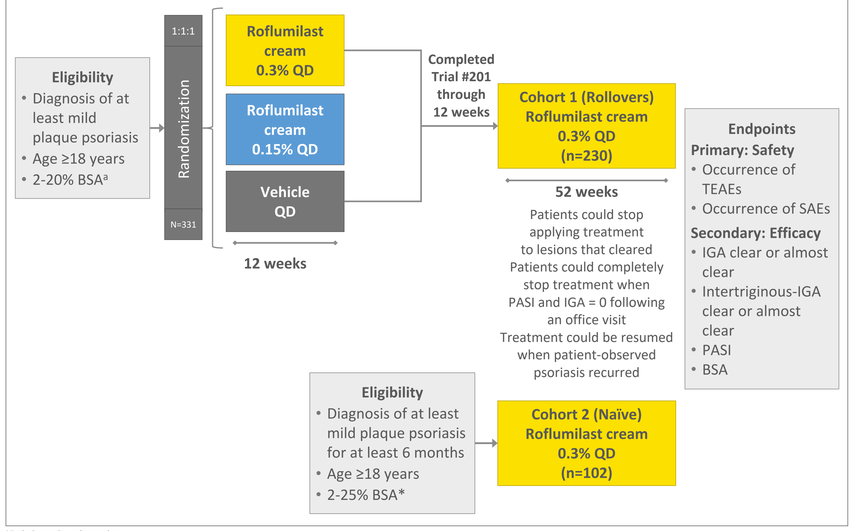
INTRODUCTION

- Roflumilast cream, a phosphodiesterase 4 (PDE4) inhibitor that is more potent than other PDE4 inhibitors,[1] was recently approved as a once-daily, nonsteroidal, topical treatment for psoriasis, including intertriginous areas, in patients 12 years of age and older with no limitations on duration of use
- In a phase 2b, randomized, double-blind, 12-week trial of 331 adults with chronic plaque psoriasis, roflumilast cream once daily was superior to vehicle cream and was well tolerated[2]
- The durability of response was assessed in a multicenter, open-label, 52-week study conducted to evaluate long-term safety of roflumilast 0.3% cream in patients with chronic plaque psoriasis

METHODS

- This multicenter, open-label, single-arm, long-term, phase 2 safety trial was conducted at 30 centers in the United States and Canada
- Two cohorts of patients were enrolled: Cohort 1 patients were those who completed the phase 2b trial through Week 12, whereas Cohort 2 eligible patients were newly enrolled (treatment-naïve; Figure 1)

Figure 1. Study Design



[a]Excludes scalp, palms, soles.
BSA: body surface area; IGA: Investigator Global Assessment; QD: once daily; PASI: Psoriasis Area Severity Index; SAE: serious adverse event; TEAE: treatment-emergent adverse event.

RESULTS

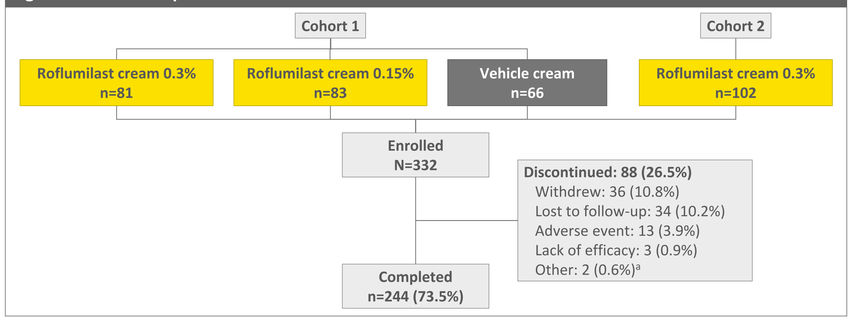
- Patient demographics and clinical characteristics at baseline were similar across cohorts (Table 1)
- Of the 249 subjects who completed trial 201 from sites that participated in this open-label trial, 230 (92.4%) of them enrolled into this study
- 244 (73.5%) completed the 202 trial of the 332 patients enrolled across cohort 1 (n=230) and cohort 2 (n=102; Figure 2)
- Percentages of patients achieving Investigator Global Assessment (IGA) Success and an IGA of Clear or Almost Clear were consistent over time (Figure 3)

Table 1. Baseline Disease Characteristics

	Roflumilast 0.15% and 0.3% → Roflumilast 0.3% (n=164)	Cohort 2 and Vehicle → Roflumilast 0.3% (n=168)	Overall Total (N=332)
BSA, mean %	6.6	6.0	6.3
PASI, mean	7.2	6.3	7.1
IGA score, n (%)			
1 (almost clear)	0 (0.0)	8 (4.8)	8 (2.4)
2 (mild)	28 (17.1)	40 (23.8)	68 (20.5)
3 (moderate)	124 (75.6)	110 (65.5)	234 (70.5)
4 (severe)	12 (7.3)	10 (6.0)	22 (6.6)
Intertriginous involvement (I-IGA ≥2)			
I-IGA, n (%)			
2 (mild)	14 (8.5)	17 (10.1)	31 (9.3)
3 (moderate)	11 (6.7)	18 (10.7)	29 (8.7)
4 (severe)	1 (0.6)	1 (0.6)	2 (0.6)

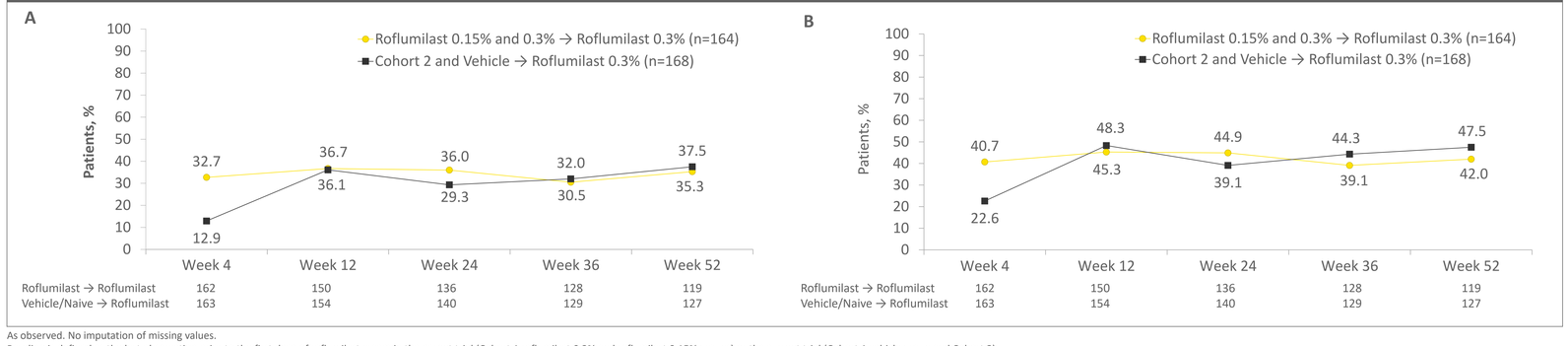
Baseline is defined as the last observation prior to the first dose of roflumilast cream in the parent trial (Cohort 1 roflumilast 0.3% and roflumilast 0.15% groups) or the current trial (Cohort 1 vehicle group and Cohort 2).
BSA: body surface area; IGA: Investigator Global Assessment; I-IGA: Intertriginous-IGA; PASI: Psoriasis Area Severity Index.

Figure 2. Patient Disposition



[a]Two patients withdrew from the study due to "other" reasons, which was COVID-19 disruption.

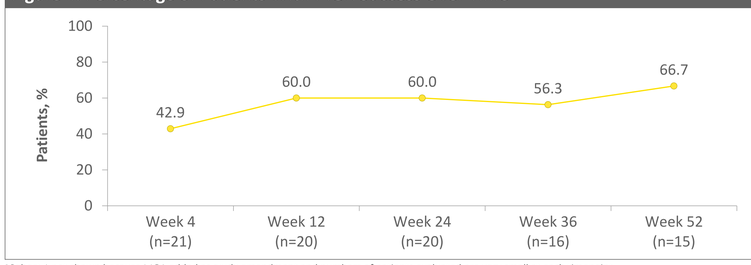
Figure 3. Percentage of Patients Achieving (A) IGA Success and (B) Clear or Almost Clear



As observed. No imputation of missing values.
Baseline is defined as the last observation prior to the first dose of roflumilast cream in the parent trial (Cohort 1 roflumilast 0.3% and roflumilast 0.15% groups) or the current trial (Cohort 1 vehicle group and Cohort 2).
IGA: Investigator Global Assessment; IGA Success = IGA score of Clear or Almost Clear plus two-grade improvement from baseline.

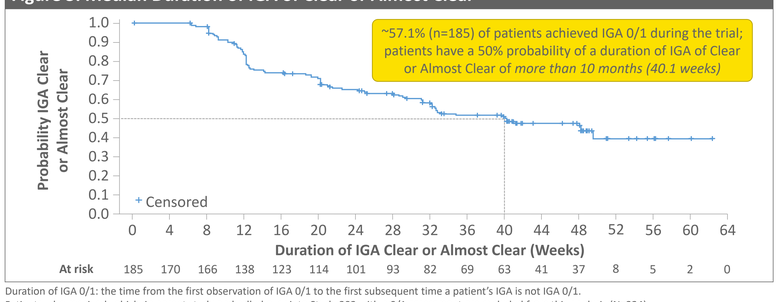
- Among patients with intertriginous area involvement, roflumilast cream provided consistent improvement of Intertriginous-Investigator Global Assessment (I-IGA; Figure 4)
- Median duration of IGA of Clear or Almost Clear was 10 months (Figure 5)
- A 60.5% mean improvement from baseline in Psoriasis Area Severity Index (PASI) and 60.1% mean improvement from baseline in body surface area (BSA) affected were observed at Week 12 (Figures 6 and 7)
  - Results were consistent through Week 52
  - Median BSA at Week 52 was 1.0%

Figure 4. Percentage of Patients With I-IGA Success Over Time[3,a]



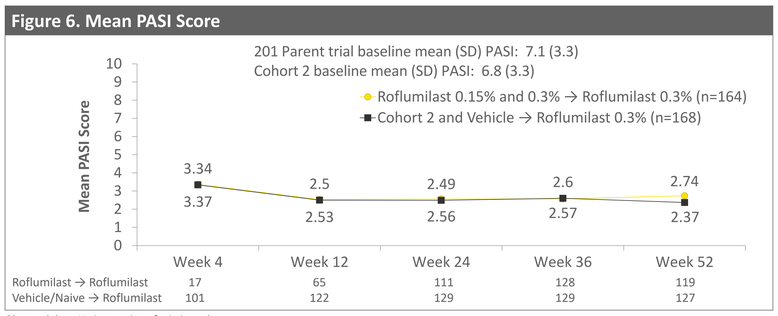
[a]Cohort 1 not shown because I-IGA added as study amendment and numbers of patients evaluated are very small at each timepoint.
I-IGA: intertriginous Investigator Global Assessment; I-IGA Success: I-IGA score of Clear or Almost Clear plus 2-grade improvement from baseline.

Figure 5. Median Duration of IGA of Clear or Almost Clear



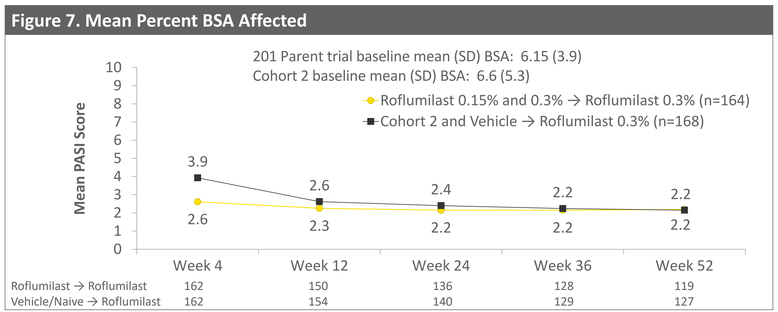
Duration of IGA 0/1: the time from the first observation of IGA 0/1 to the first subsequent time a patient's IGA is not IGA 0/1.
Patients who received vehicle in parent study and rolled over into Study 202 with a 0/1 assessment are excluded from this analysis (N=324).
IGA: Investigator Global Assessment.

Figure 6. Mean PASI Score



Observed data. No imputation of missing values.
PASI assessment was added as an amendment to the trial.
PASI: Psoriasis Area and Severity Index; SD: standard deviation.

Figure 7. Mean Percent BSA Affected



Observed data. No imputations of missing values.
Baseline is defined as the last observation prior to the first dose of Roflumilast Cream in the ARQ-151-202 study.
BSA: body surface area; SD: standard deviation.

- Safety was consistent with the parent trial (Tables 2 and 3)
- 94% of adverse events (AEs) were rated mild or moderate in severity
- 97% of AEs were unrelated or unlikely to be related to treatment as determined by the investigator
- ≥97% of patients had no evidence of irritation per investigator local tolerability assessment at each visit (Figure 8)

Table 2. Summary of AEs (Safety Population)

TEAE, n (%)	Roflumilast 0.15% and 0.3% → Roflumilast 0.3% (n=164)	Cohort 2 and Vehicle → Roflumilast 0.3% (n=168)	Overall (N=332)
Patients with any TEAE	79 (48.2)	85 (50.6)	164 (49.4)
Patients with any treatment-related TEAE	4 (1.7)	5 (4.9)	9 (2.7)
Patients with any SAE	8 (4.9)	4 (2.4)	12 (3.6)
Any treatment-related SAE	0 (0)	0 (0)	0 (0)
Patients who discontinued study drug due to AE	8 (4.9)	5 (3.0)	13 (3.9)

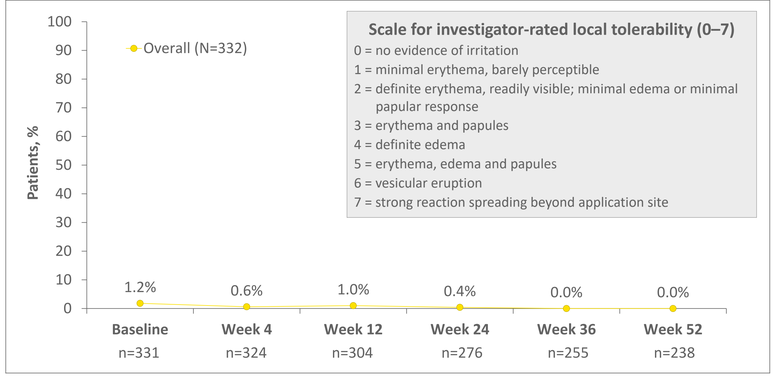
Treatment-emergent adverse event defined as event with an onset on or after the date of the first study drug application in ARQ-151-202 study.
AE: adverse event; SAE: serious adverse event; TEAE: treatment-emergent adverse event.

Table 3. Most Common AEs (>2% Overall)

TEAE, n (%)	Roflumilast 0.15% and 0.3% → Roflumilast 0.3% (n=164)	Cohort 2 and Vehicle → Roflumilast 0.3% (n=168)	Overall (N=332)
Upper respiratory tract infection/ viral URTI	10 (6.1)	12 (7.1)	22 (6.6)
Nasopharyngitis	6 (3.7)	6 (3.6)	12 (3.6)
Urinary tract infection	5 (3.0)	6 (3.6)	11 (3.3)
Sinusitis	3 (1.8)	5 (3.0)	8 (2.4)

AE: adverse event; TEAE: treatment-emergent adverse event; URTI: upper respiratory tract infection.

Figure 8. Percentage of Patients With Investigator-rated Tolerability Score >0



CONCLUSIONS

- In this phase 2 long-term safety study, roflumilast cream 0.3%, a once-daily, nonsteroidal topical PDE4 inhibitor, was well-tolerated with a safety profile consistent with the parent phase 2b trial (Trial 201)
  - Rates of discontinuations due to AEs and lack of efficacy were low
  - No tachyphylaxis occurred and efficacy was consistent over time (IGA Success, IGA 0/1, and percentage change from baseline in BSA and PASI)
  - Of the 185 patients who achieved IGA Clear/Almost Clear during the open-label trial, the median durability of IGA of Clear/Almost Clear was 10 months (40.1 weeks)

REFERENCES

1. Dong C, et al. *J Pharmacol Exp Ther* 2016;358:413–422.
2. Lebwohl MG, et al. *N Engl J Med* 2020;383:229–239.
3. Stein Gold LS, et al. Poster presented at: Innovations in Dermatology; March 16-20, 2021; Virtual.

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DISCLOSURES

ML, LSG, MJG, KAP, LKF, DNA, HCH, LHK, and **MZ** are investigators and/or consultants for Arcutis Biotherapeutics, Inc. and received grants/research funding and/or honoraria; **PB, RH, DK,** and **DB** are employees of Arcutis Biotherapeutics, Inc. Additional disclosures provided on request.